PATENT COOPERATION TREATY

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

25/8

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/IN2005/000011	International filing date *(day/month/year)* 07.01.2005
Priority date *(day/month/year)* 09.01.2004	
International Patent Classification (IPC) or both national classification and IPC C07D405/06, C07D319/06, C07D413/06, C07D495/04, C07D417/06, C07D407/06, A61K31/357, A61P3/04,	
Applicant CADILA HEALTHCARE LIMITED	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IN2005/000011

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IN2005/000011

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 5(part),7-10

because:

☒ the said international application, or the said claims Nos. 7-10 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 5(part) are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 5(part)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IN2005/000011

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	5
	No:	Claims	1-4,6-11
Inventive step (IS)	Yes:	Claims	5
	No:	Claims	1-4,6-11
Industrial applicability (IA)	Yes:	Claims	1-6,11
	No:	Claims	

2. Citations and explanations

see separate sheet

III. Non-establishment of opinion

Claims 7-10 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

There are 2 claims numbered "3" and no claim 5. The following examination has been based on the claims wherein the 2nd claim presently numbered "3" is treated as claim 4 and present claim 4 is renumbered as claim 5.

A number of examples (3, 12, 17, 26, 35, 37, 48) do not fall within the scope of formula (I) of present claim 1. These examples are claimed in claim 5 as being compounds of claims 1-3. This introduces a contradiction into the claims, which creates a lack of clarity (Article 6 PCT) concerning the scope of the claims. Only formula (I) has been searched, thus no opinion will be established for those compounds of claim 5 not falling within this formula.

V. Reasoned statement

Reference is made to the following documents:
D1: EP-A-1 295 875
D2: Albany Molecular Research, Inc. Technical Reports, vol. 7, no. 46, 2002, p. 8-9
D3: WO00/04011

Novelty

In claim 1 compounds wherein A is i.a. optionally substituted heteroaryl or optionally substituted heterocyclyl are claimed. Thus it is clear that the term "heterocyclyl" does not include heteroaryl - if it did, both possibilities would not be separately listed in the claim. In proviso i) compounds wherein A is heterocyclyl having aryl, aromatic, heterocyclic or cycloalkyl substituents are excluded. No mention is made of an exclusion of compounds wherein A is heteroaryl having these substituents. D1 discloses a general formula [1] wherein the group corresponding to the present A is a divalent aromatic heterocyclic group, i.e. a heteroaryl group. This disclosure overlaps with the present claims. The compounds are described as being effective at lowering

triglyceride, LDL-C and insulin levels in the blood and can thus be useful in the treatment of i.a. diabetes and obesity. Furthermore, D1 discloses specific compounds falling within the scope of the present claims (e.g. the compounds of examples 1-4). D2 elaborates on the mechanism of action of one of the compounds of D1, stating that it is a selective PPAR-alpha activator.
These disclosures are novelty-destroying for present claims 1-4 and 6-11.
D3 discloses general formula I wherein R^2 or R^3 may be $(C_6\text{-}C_{10})$aryl$(C_1\text{-}C_7)$alkyl wherein the aryl group may optionally be substituted. In present claim 1, proviso ii) excludes certain compounds wherein A is a substituted aryl group, however there is no exclusion of compounds wherein A is an unsubstituted aryl group. The compounds of D3 are described as being activators of PPAR-alpha and gamma, useful as hypolipidemic and hpyoglycemic agents. Thus the disclosure of D3 overlaps with present claims 1, 3 and 7-10.
Claims 1-4 and 6-11 do not fulfil the requirements of Article 33(2) PCT.

Inventive step

In view of their lack of novelty, claims 1-4 and 6-11 cannot be inventive.
Re. those compounds of claim 5 which fall within the scope of formula (I):
For those compounds wherein A is heterocyclic or heteroaryl, D1 is taken as the closest prior art. The compounds of D1 all have 2 rings directly attached to one another (R^1-Het-). None of the compounds of claim 5 have this feature. It does not appear obvious to provide further compounds with PPAR modulating activity by replacing the R^1 ring of D1 by one of the substituents given in claim 5. Thus for the compounds wherein A is heterocyclic or heteroaryl, claim 5 may be considered inventive.
For the compounds wherein A is aryl, D3 may be taken as the closest prior art. The compounds of claim 5 differ in the identity of the substituent on the aryl group. The structurally closest compounds are ex. 18 and 19, which possess a phenyl ring substituted by a benzyloxy group and a methanesulfonyloxy group, whereas the compounds of D3 may have an aryl group substituted by a hydroxy group, a trifluoromethoxy group or alkoxy group. In the absence of any teaching that the substituents of present claim 5 and those of D3 are equivalent in compounds with PPAR modulating activity, it does not appear to be obvious to provide further compounds with this activity by modifiying the compounds of D3 in the way claimed.

Thus the compounds of claim 5 which fall within the scope of claim 1 and which have the alleged activity may be considered inventive.
Claims 1-4 and 6-11 do not fulfil the requirements of Article 33(3) PCT.
Claim 5 fulfil the requirements of Article 33(3) PCT.

Industrial applicability

Claims 1-6 and 11 fulfil the requirements of Article 33(4) PCT.
No unified criteria exist in the PCT Contracting States for assessing whether present claims 7-10 are industrially applicable. The patentability can be dependent upon the formulation of the claims. For example, the EPO does not consider claims to the use of a compound in medical treatment to be industrially applicable, but allows claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.